The structures were solved by direct methods and refined by full-matrix least squares for all reflections. H atoms were placed geometrically (except those of the H_2O molecules in BRL-53888A, which were obtained from a difference Fourier synthesis) and refined with a riding model and with U_{iso} constrained to be $1.25U_{eq}$ of the parent atom.

For both compounds, data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structures: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PARST* (Nardelli, 1983).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1280). Services for accessing these data are described at the back of the journal.

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4-Ethyl-2,3-dihydro-4*H*-pyrido[3,2-*e*]-1,2,4-thiadiazine 1,1-dioxide and 4-ethyl-2,3-dihydro-4*H*-pyrido[4,3-*e*]-1,2,4-thiadiazine 1,1-dioxide†

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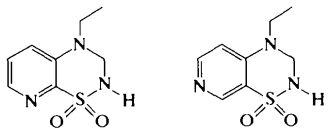
Abstract

A series of 4*H*-1,2,4-pyridothiadiazine 1,1-dioxides and 2,3-dihydro-4*H*-1,2,4-pyridothiadiazine 1,1-dioxides were tested as possible allosteric modulators of the (*R/S*)-2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl) propionic acid receptors; the most active is 4-ethyl-2,3-dihydro-4*H*-pyrido[3,2-*e*]-1,2,4-thiadiazine 1,1-dioxide, $C_8H_{11}N_3O_2S$. Its crystal molecular geometry is compared with that of the -pyrido[4,3-*e*]- compound, $C_8H_{11}N_3O_2S$, a less potent analogue.

Comment

A series of 4*H*- and 2,3-dihydro-4*H*-1,2,4-pyridothiadiazine 1,1-dioxides, belonging to three different chemical classes (as a function of the N-atom position in the heterocycle) and bearing various alkyl and aryl substituents at the 2, 3 and 4 positions, were synthesized and tested as possible allosteric modulators of the (*R/S*)-2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl) propionic acid (AMPA) receptors. Many compounds were found to be more potent than the reference compounds diazoxide (Bandoli & Nicolini, 1977) and aniracetam as potentiators of the AMPA current in rat cortex mRNA-injected *Xenopus* oocytes. The most active compound, 4-ethyl-2,3-dihydro-4*H*-pyrido[3,2-*e*]-1,2,4-thiadiazine 1,1-dioxide, (1), revealed an *in vitro* activity not far from that of cyclothiazide, the most potent allosteric modulator of AMPA receptors reported to date. Structure–activity relationships were deduced and indicated the possible dissociation between the structure requirements leading to a biological activity

† Systematic names: 4-ethyl-3,4-dihydro-2*H*-pyrido[3,2-*e*]-1,2,4-thiadiazine 1,1-dioxide and 4-ethyl-3,4-dihydro-2*H*-pyrido[4,3-*e*]-1,2,4-thiadiazine 1,1-dioxide.



(1) (2)

of the pyridothiadiazines even on AMPA receptors or on ATP-sensitive K^+ channels (Pirotte *et al.*, 1998).

The crystal structure of (1) exhibits two independent conformers, (1*A*) and (1*B*), in the asymmetric unit which are distinguishable by the different orientations of the terminal methyl group of the side chains. N2 was found to be clearly of sp^3 pyramidal geometry [sums of bond angles around N2 are 336 (2) and 328 (2)° for conformers (1*A*) and (1*B*), respectively] whereas N4 was found to be of sp^2 geometry [sums of bond angles around N4 are 359.3 (3) and 356.7 (3)° for (1*A*) and (1*B*), respectively].

4-Ethyl-2,3-dihydro-4*H*-pyrido[4,3-*e*]-1,2,4-thiadiazine 1,1-dioxide, (2), crystallizes with one molecule in the asymmetric unit geometrically superimposable to conformer (1*A*). N2 approximates the sp^3 pyramidal geometry [sum of angles is 337 (2)°] and N4 coincides with an sp^2 geometry [sum of angles is 360.0 (2)°]. Compound (2) shows a strong analogy with the previously reported 2,4,7-trimethyl-2,3-dihydro-4*H*-pyrido[4,3-*e*]-1,2,4-thiadiazinium 1,1-dioxide iodide (Dupont *et al.*,

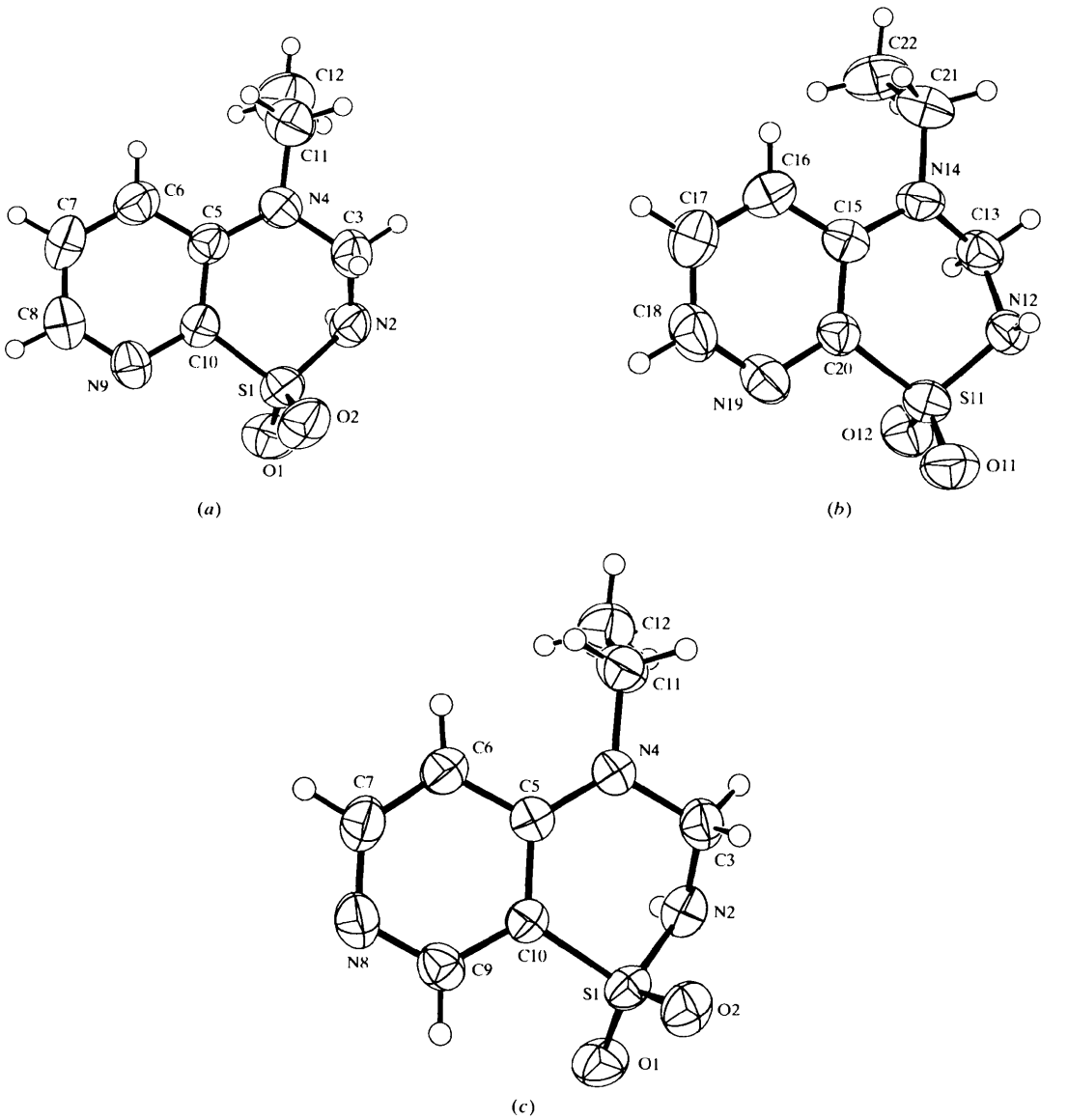


Fig. 1. Molecular structure with atom-labelling scheme for (*a*) molecule (1*A*), (*b*) molecule (1*B*) and (*c*) molecule (2). Displacement ellipsoids are shown at 50% probability levels. H atoms are drawn as small circles of an arbitrary radius.

1995) bearing a methyl group on the N atom at the 2 position [angles around N2 and N4 are 341.8 (9) and 359.6 (9)°, respectively].

A comparison of the molecular geometries of (1) and (2) shows no significant variation. In particular, the sp^3 nature of N at the 2 position of the thiadiazine diazoxide ring is almost similar in both structures. Hence the difference in their biological activity is primarily due to the nitrogen position in the pyridine ring.

The shortest intermolecular contacts include NH on the 2 position in both structures (Tables 2 and 4). In (1*A*) and (2), the geometries agree with nearly 'linear' NH···O or NH···H hydrogen bonds. In (1*B*) the N12···O2 and N12···N9 intermolecular distances are close to the sum of their respective van der Waals radii. In this case, the occurrence of an asymmetric 'bifurcated' hydrogen bond may be tentatively suggested (Taylor *et al.*, 1984).

Experimental

The compounds were synthesized at the Laboratory of Medicinal Chemistry of Liège (Pirotte *et al.*, 1998). Crystals were obtained by slow evaporation of a methanol solution at room temperature.

Compound (1)

Crystal data

$C_8H_{11}N_3O_2S$
M_r = 213.26
Monoclinic
$P2_1/n$
a = 7.7385 (12) Å
b = 12.199 (3) Å
c = 20.667 (2) Å
β = 99.735 (18)°
V = 1922.9 (6) Å^3
Z = 8
D_x = 1.473 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54180 Å
Cell parameters from 27 reflections
θ = 26.14–37.34°
μ = 2.839 mm^{-1}
T = 293 (2) K
Prismatic
0.46 × 0.30 × 0.23 mm
Colourless

Data collection

Stoe–Siemens AED four-circle diffractometer
ω scans
Absorption correction: semi-empirical, ψ scans (*EMPIR*; Stoe & Cie, 1987*a*)
T_{min} = 0.294, T_{max} = 0.341
3719 measured reflections
3451 independent reflections

1937 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 67.47°
$h = -9 \rightarrow 9$
$k = -3 \rightarrow 14$
$l = -24 \rightarrow 24$
2 standard reflections
frequency: 60 min
intensity decay: 4.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.132
S = 0.943
3451 reflections
262 parameters
H atoms were restrained (included as riding atoms) and atoms H2 and H12 were refined
$w = 1/[\sigma^2(F_o^2) + (0.0819P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.343 e Å^{-3}
$\Delta\rho_{min}$ = −0.239 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.0166 (8)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °) for (1)*

S1—N2	1.632 (3)	S11—N12	1.627 (3)
N2—C3	1.432 (5)	N12—C13	1.462 (4)
N2—H2	0.87 (3)	N12—H12	0.88 (3)
C3—N4	1.443 (4)	C13—N14	1.452 (4)
N4—C5	1.376 (4)	N14—C15	1.372 (4)
N4—C11	1.466 (5)	N14—C21	1.459 (4)
N2—S1—C10	102.06 (15)	N12—S11—C20	102.00 (14)
C3—N2—S1	113.9 (2)	C13—N12—S11	112.9 (2)
C3—N2—H2	122 (2)	C13—N12—H12	113 (2)
S1—N2—H2	100 (2)	S11—N12—H12	103 (2)
N2—C3—N4	113.6 (3)	N14—C13—N12	111.9 (3)
C5—N4—C3	118.2 (3)	C15—N14—C13	117.8 (2)
C5—N4—C11	123.6 (3)	C15—N14—C21	121.5 (3)
C3—N4—C11	117.5 (3)	C13—N14—C21	117.4 (3)
N4—C11—C12	111.9 (3)	N14—C21—C22	114.0 (3)
C10—S1—N2—C3	42.7 (3)	C20—S11—N12—C13	−43.4 (2)
S1—N2—C3—N4	−65.5 (4)	S11—N12—C13—N14	67.5 (3)
N2—C3—N4—C5	46.9 (4)	N12—C13—N14—C15	−52.7 (4)
N2—C3—N4—C11	−142.2 (3)	N12—C13—N14—C21	147.4 (3)
C3—N4—C5—C10	−9.5 (5)	C13—N14—C15—C20	17.6 (4)

Table 2. *Hydrogen-bonding geometry (Å, °) for (1)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O12^{i}	0.87 (3)	2.25 (3)	3.034 (4)	149 (3)
N12—H12···O2^{ii}	0.88 (3)	2.80 (3)	3.285 (3)	116 (3)
N12—H12···N9^{ii}	0.88 (3)	2.47 (3)	3.305 (4)	159 (3)

Symmetry codes: (i) $1 + x, y, z$; (ii) $x - \frac{1}{2}, \frac{3}{2} - y, \frac{1}{2} + z$.

Compound (2)

Crystal data

$C_8H_{11}N_3O_2S$
M_r = 213.26
Monoclinic
$P2_1/n$
a = 8.1628 (4) Å
b = 11.6259 (8) Å
c = 10.2405 (11) Å
β = 97.841 (7)°
V = 962.74 (13) Å^3
Z = 4
D_x = 1.471 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54180 Å
Cell parameters from 32 reflections
θ = 29.96–37.23°
μ = 2.835 mm^{-1}
T = 293 (2) K
Prismatic
0.46 × 0.42 × 0.38 mm
Colourless

Data collection

Stoe–Siemens AED four-circle diffractometer
ω scans
Absorption correction: semi-empirical, ψ scans (*EMPIR*; Stoe & Cie, 1987*a*)
T_{min} = 0.329, T_{max} = 0.520
1803 measured reflections
1707 independent reflections

1387 reflections with $I > 2\sigma(I)$
R_{int} = 0.038
θ_{max} = 68.01°
$h = -9 \rightarrow 9$
$k = -13 \rightarrow 0$
$l = 0 \rightarrow 12$
2 standard reflections
frequency: 60 min
intensity decay: 2.6%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.106$
$S = 1.060$
1707 reflections
132 parameters
H atoms were restrained (included as riding atoms) and atom H2 which was refined
$w = 1/[\sigma^2(F_o^2) + (0.0469P)^2 + 0.5899P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.215$ e Å^{-3}
$\Delta\rho_{min} = -0.265$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.0260 (14)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 3. *Selected geometric parameters (Å, °) for (2)*

S1—N2	1.627 (2)	C3—N4	1.463 (3)
N2—C3	1.435 (3)	N4—C5	1.353 (3)
N2—H2	0.75 (3)	N4—C11	1.465 (3)
N2—S1—C10	100.97 (11)	C5—N4—C3	121.4 (2)
C3—N2—S1	111.66 (17)	C5—N4—C11	122.9 (2)
C3—N2—H2	115 (2)	C3—N4—C11	115.7 (2)
S1—N2—H2	110 (2)	N4—C11—C12	112.0 (2)
N2—C3—N4	113.7 (2)		
C10—S1—N2—C3	54.77 (19)	N2—C3—N4—C11	−150.9 (2)
S1—N2—C3—N4	−63.6 (3)	C3—N4—C5—C10	1.7 (4)
N2—C3—N4—C5	32.5 (3)		

Table 4. *Hydrogen-bonding geometry (Å, °) for (2)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···N8^{i}	0.75 (3)	2.20 (3)	2.937 (3)	168 (3)

Symmetry code: (i) $\frac{1}{2} - x, y - \frac{1}{2}, \frac{1}{2} - z$.

For both compounds, data collection: *DIF*4 (Stoe & Cie, 1987*b*); cell refinement: *DIF*4; data reduction: *REDU*4 (Stoe & Cie, 1987*c*); program(s) used to solve structures: *SHELXS*97 (Sheldrick, 1997*b*); program(s) used to refine structures: *SHELXL*97 (Sheldrick, 1997*a*); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97.

The authors thank M. M. Vermeire for his helpful assistance in the diffractometry measurements and the Belgian FNRS (Fonds National de la Recherche Scientifique) for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1021). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 464–466

2,3,7,8,12,13,17,18-Octafluoro-5,10,15,20-tetrakis(pentafluorophenyl)porphyrin

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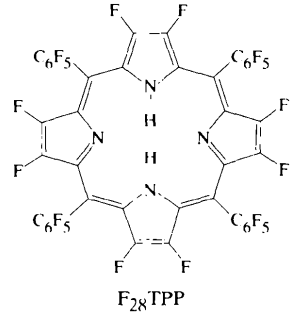
Abstract

The core of the title compound, $C_{44}H_2F_{28}N_4$, is essentially planar while the pentafluorophenyl groups are nearly perpendicular to the mean porphyrin plane. The molecule is centrosymmetric.

Comment

The title compound, F_{28}TPP, was prepared as part of a study of β-octafluoroporphyrins (Leroy *et al.*, 1997), a new class of highly electron-deficient ligands. The crystal structure of F_{28}TPP (Fig. 1) was determined, amongst others, in an attempt to correlate this porphyrin structure with the unusual spectroscopic data observed.



F_{28}TPP